REMARKS

Further and favorable reconsideration is respectfully requested in view of the foregoing amendments and following remarks.

Thus, the specification has been amended as suggested by the Examiner, thus rendering the objection to the disclosure moot.

Claim 1 has been amended to recite that the polymer substrate is a water-insoluble graft polymer substrate, on the basis of the disclosure at, for example, page 8, lines 24-25 of the specification.

Attached hereto is a marked-up version of the changes made to the Specification and claim 1 by the current amendment. The attached pages are captioned "**Version with markings to show changes made.**"

New claims 30-31 have been added to the application.

New claim 30 recites how the graft polymer is produced, attention in this regard being directed to page 10, lines 2-19 and page 11, lines 3-4 of the specification.

New claim 31 corresponds to a combination of claims 16 and 29. In this regard, Applicants note that the Examiner indicates that claim 16 is objected to as dependent on a rejected claim. Claims 16 and 29 have been canceled, and new claim 31 is considered to be allowable.

The patentability of the present invention over the disclosures of the references relied upon by the Examiner in rejecting the claims will be apparent upon consideration of the following remarks.

Thus, the rejection of claims 1-9, 11 and 23-26 under 35 U.S.C. § 102(b) as being anticipated by Patnaik et al. is respectfully traversed.

The effective date of the Patnaik et al. reference as prior art is its U.S. filing date of November 25, 1996. This date is subsequent to Applicants' Japanese priority date of October 15, 1996. Therefore, obtaining the benefit of the priority date will be effective to overcome the use of this reference as prior art against the present invention, as recognized by the Examiner.

Accordingly, Applicants are submitting herewith a verified English translation of their priority application, which they submit overcomes the use of the Patnaik et al. reference as prior art.

The rejection of claims 1-9, 11, 23-26 and 29 under 35 U.S.C. § 102(b) as being anticipated by Guire is respectfully traversed.

As indicated above, the polymer substrate employed in the present invention is a water-insoluble graft polymer substrate. This makes the surface of the polymer substrate much more reactive, thus facilitating linkage between the polymer substrate and the biologically active compound. There is absolutely no disclosure or suggestion of a water-insoluble graft polymer substrate in the Guire reference, as a result of which the presently claimed invention is considered to be patentable over this reference.

Therefore, in view of the foregoing amendments and remarks, it is submitted that each of the grounds of objection and rejection set forth by the Examiner has been overcome, and that the application is in condition for allowance. Such allowance is solicited.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

Please rewrite the paragraph on page 2, lines 2-25 as follows:

Under these circumstances, where raw materials for agriculture, forestry and fishery, and foods are manufactured in large quantities, chemotherapeutics that were originally developed for the emergency treatment of human or animal subjects are used as such, or used after their partial modifications; and organic, synthetic agrochemical with low selectivity of action (insecticides, bactericides, herbicides, oyster-attaching preventers, and the like [etc.]) are used. This not only gives drug-induced sufferings, which can not be ignored, to those other than the targets, but also induces the appearance of tolerant organisms due to the diffusion of the drugs within an environment. A serious danger is thus pointed out that the drugs, which were developed for the emergency treatment of humans, can no longer be employed in their intended therapeutic use. In other words, drug-resistance, especially resistance to a great variety of antibiotics (multiple drug resistance) prevails among the group of non-pathogenic microorganisms that constitutes an overwhelming majority in the ecological system of nature, and it is also amplifying propagation of the multiple drug resistance among pathogenic bacteria, directly or indirectly: such possibility is apprehended. (M. Yoshikawa, Bull. of Jap. Soc. of Microbial Ecology, 10, No. 3, 141-148 (1995).)

Please rewrite the paragraph from page 3, line 26 to page 4, line 18 as follows:

In the traditional concept in pharmaceutical sciences, it has been fundamentally believed that drugs can not exert their intrinsic effects if they have been converted to the immobilized state, and that they can do so only in cases where they are used in their free state. Accordingly, no provisions exist in the laws and rules of the world pertaining to the manufacture, the use, the approval, and the like [etc.] of drugs that deal with drug-immobilized polymer substrate preparations in which low-molecular weight drugs are allowed to be linked to polymer substances so as not to cause liberation of the drugs and which can exert therapeutic effects without involving the liberation. To put it differently, in the case of medicinal preparations where low-molecular weight drugs are immobilized to polymer substances, it has been believed that the liberation of the drugs is an essential prerequisite when they are allowed to act on targets like the controlled-releasing preparations stated above. It

can be said that there has been no need to make the controlling laws and regulations, because the drugs have been believed to be totally ineffective if their liberation does not occur.

Please rewrite the paragraph on page 14, lines 11-26 as follows:

Here, the expression "exerts (the) selective biological activity" means that substantially no harm or tolerable adverse reactions are brought to a host environment (nature, a host animal or plant, cells, and organelle, and the like [etc.]) and that the biological activity is exerted against a harmful, target agent the elimination or the control of which is wanted. Therefore, chemotherapeutics are mentioned as the biologically active compounds exerting their selective biological activity. The chemotherapeutics are drugs having high selective toxicity that causes only damage to harmful agents to be targeted without damaging hosts. The objects of chemotherapeutics are not limited to living things such as pathogenic microorganisms or harmful animals and plants, but extend to a considerably wide range, including cells such as malignant tumors, and non-living matters such as enzymes, receptors, and hormones.

Please rewrite the paragraph on page 18, lines 8-16 as follows:

Among preferable drugs which can be utilized in this invention, those described below can be illustrated as the most important chemotherapeutics:
griseofluvin, vernamycin B, ostreogrycin G, isoniazid, benzonaphtacequinones such as benanomicin and pradimicin, pyridoxine, PAS, pimaricin, fungichromin, formycin, toyocamycin, chloramphenicol, tetracycline, streptomycin, erythromycin, ampicillin, norcardicin, SQ 83360, and OA-6129, and the like [etc].

Please rewrite the paragraph on page 21, lines 2-10 as follows:

Mentioned as other organic polymers are natural organic polymers and modified natural organic polymers, which have been conventionally used to form the substrates for gel filtration, ion-exchange chromatography, affinity chromatography or the like. To specifically name these: cellulose, agarose, glucomannan, chitosan, pullulan, starch, dextran, and the like [etc]. Conventionally, the

substrates for use in affinity chromatography and the like have been processed as porous spheres of these natural organic polymers.

Please rewrite the paragraph from page 25, line 24 to page 26, line 7 as follows:

The functional groups that can be used at "the active site provided on the substrate," or at "the active site provided at the graft chain branched from the substrate," or at "both termini of the spacer (may not be the same groups)," or at "the specified position of the biologically active compound for linking" and that can be mentioned are, for example, as follows:
a double bond, a triple bond, an amino group, an epoxy group, a glycyl group, an isocyanate group, an aldehyde group, a carboxyl group or a derivative thereof (e.g., an ester group, an anhydrous carboxylic acid group and a halogenated carbonyl group), an allyl group, and the like [etc].

Please rewrite the paragraph from page 28, line 22 to page 29, line 2 as follows:

When R^1 is a cation, it represents a carboxylate. The cation is not particularly limited, and may be either an inorganic cation or an organic cation. Mentioned as the inorganic cation are an alkaline metal cation such as sodium ion or potassium ion, an alkaline earth metal ion such as calcium ion, a transition metal ion such as ferric ion (or ferrous ion), a complex ion, and the like [etc]. Mentioned as the organic ion is, for example, an ammonium ion such as a tetraalkylammonium ion.

Please rewrite the paragraph from page 32, line 27 to page 33, line 9 as follows:

Further, in this invention the immobilization of a biologically active compound has a purpose of preventing the biologically active compound from freely moving and diffusing within its environment. Therefore, when the biologically active compound is immobilized to the spherical substrate described above, it is preferred that the immobilization be conducted so that the spherical substrate may not disperse into the treatment space (e.g., a filtration bed provided on the passageway for filtering the air containing treatment objects) of objects to be treated (bacteria, molds, and the like [etc]).

Please rewrite the paragraph from page 40, line 27 to page 41, line 5 as follows:

Another example of utilization of the biologically active polymer products of this invention is use forms that suppose the use for considerably long hours. For example, the polymer products of the invention that have bees processed into sheet forms, paint forms, or fibrous forms may be utilized as clothes, curtains, sheets, paint products, external films, sanitary goods, and the like [etc].

Please rewrite the paragraph from page 41, line 24 to page 42, line 12 as follows:

A nonwoven fabric having a METSUKE (weight per unit area) of 50 g/m^2 and a thickness of 0.4 mm, which was made of polypropylene (available from Mitsui Petrochemical Ind. Co.; the trade name: Syntex PS-110), was irradiated 200 kGy with electron beam (at 2 Mev and 1 mA) under a nitrogen atmosphere. Then, these fibers were immersed in a monomer solution of acrylic acid/methanol (1/9) and were allowed to react at 40°C for 4 h. Consequently, fibers having an acrylic acid graft rate of 78.5% were produced, which are hereinafter referred to as the "grafted fibers with carboxyl groups." The ion-exchange capacity of the grafted fibers with carboxyl groups was 6 meq/g. Here, the graft rate was calculated according to the following formula:

graft rate={(weight of substrate after graft formation- weight of substrate before graft formation)/ weight of substrate before graft formation}x100(%)

Please rewrite the paragraph from page 44, line 10 to page 45, line 5 as follows:

FIG. 2 shows the results from a test of antimicrobial activity of these ampicillin-immobilized sample and control sample against Staphylococcus aureus FDA 209P, as assayed by the rapid evaluation method for antibiotic activities. As is apparent from FIG. 2, the sample having immobilized ampicillin in the presence of carbodiimide displays distinct antimicrobial activity, whereas the sample having undergone similar treatment in the absence of carbodiimide displays no antimicrobial activity at all. This demonstrates that non-specific adsorption of ampicillin to the substrate has not occurred under the immobilization and aftertreatment conditions used here. Further, under similar testing and evaluation conditions, this ampicillin-immobilized grafted fibers with carboxyl groups displayed antimicrobial activity against Bacillus subtilis ATCC6623, Bacillus anthracis, Staphylococcus aureus K2, Staphylococcus aureus Smith, and Mycrococcus luteus

ATCC9341, and the like [etc]. However, even this ampicillin-immobilized sample was ineffective against Escherichia coli NIHJ, Proteus vulgaris OX-19, Klebsiella pneumoniae PCI602, Candida albicans 3143, Aspergillus niger, etc. Namely, it can be said that the ampicillin-immobilized grafted fibers with carboxyl groups according to this invention exert the selective biological activity that is peculiar to ampicillin.

1. (Thrice Amended) A biologically active polymer product having:

a water-insoluble graft polymer substrate; and

a biologically active compound moiety having a molecular weight of not more than 5,000, the moiety being covalently bonded to the polymer substrate and exerting selective biological activity,

wherein the biologically active compound moiety exerts the selective biological activity while being covalently bonded to the polymer substrate.